CPTO
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CLAIM 1 (ORIGINAL)

1. A polypeptide self-antigen useful as a tumor-specific vaccine in a subject with a tumor or at risk of developing a tumor, encoded at least in part by a nucleic acid in the cells of said tumor, which polypeptide:

(a) includes an epitope or epitopes unique to, or overexpressed by, cells of said tumor, thereby distinguishing said tumor from all other tumors (i) of the same or different histological type, (ii) in said subject or in another member of said subject's species;

(b) is produced in a cell or organism that has been transformed or transfected with said nucleic acid derived from said tumor of said subject;

(c) is obtainable from said cell or organism in correctly folded form, without a need for denaturation and renaturation and mimics said epitope or epitopes in their native form;

(d) is capable of inducing an immune response in a mammal, including said subject, without a need for adjuvant or other immunostimulatory materials, so that administration of said polypeptide results in an antibody or cell-mediated immune response to said epitope or epitopes.

CLAIM 2 (ORIGINAL)

2. The polypeptide of claim 1 which is produced in a plant.

CLAIM 3 (ORIGINAL)

3. The polypeptide of claim 21 which is produced transiently in said transformed or transfected plant.

CLAIM 4 (ORIGINAL)

4. The polypeptide of claim 2 which comprises at least two peptide domains.

CLAIM 5 (ORIGINAL)

5. The polypeptide of claim 2 wherein the tumor is a B-cell lymphoma and said tumor epitope is a surface immunoglobulin epitope.

CLAIM 6 (ORIGINAL)

6. The polypeptide of claim 5 that includes at least one idiotypic epitope of the V region of said immunoglobulin.

CLAIM 7 (ORIGINAL)

7. The polypeptide of claim 6 that comprises two V region domains of said immunoglobulin.

CLAIM 8 (ORIGINAL)

8. The polypeptide of claim 7 wherein said two domains are at least part of the V_H and at least part of the V_L domains of said immunoglobulin.

CLAIM 9 (ORIGINAL)

9. The polypeptide of claim 8, wherein said part of the V_H region includes at least one complementarity-determining region (CDR)

CLAIM 10 (ORIGINAL)

10. The polypeptide of claim 9, wherein said CDR is CDR2.

CLAIM 11 (ORIGINAL)

11. The polypeptide of claim 8 that is a two-domain single chain antibody (scFv) that includes said at least part of the V_H and the V_L domains.

CLAIM 12 (ORIGINAL)

12. The polypeptide of claim 11 that includes said V_H and the V_L domains.

CLAIM 13 (ORIGINAL)

13. The polypeptide of claim 12 wherein said domains are linked by an amino acid linker that

(a) has between one and about 50 residues;

(b) consists of between one and 12 different amino acids, and

(c) facilitates secretion and correct folding of said polypeptide to mimic the tumor epitope in its native form in or on said tumor cell.

CLAIM 14 (ORIGINAL)

14. The polypeptide of claim 13 wherein the linker is a member of a randomized library of linkers that vary in size and sequence, and said library is encoded by nucleic acid sequences consisting of a repeated pattern of degenerate repeated triplet nucleotides having the following requirements;

(i) position 1 of each repeated triplet cannot be the same nucleotide as position 2 of the repeated triplet;

(ii) position 2 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet; or

(iii) position 1 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet.

CLAIM 15 (ORIGINAL)

15. The polypeptide of claim 14, wherein the nucleotide in the first and second positions of each repeated triplet is selected from any two of deoxyadenosine, deoxyguanosine, deoxycytidine or deoxythymidine.

CLAIM 16 (ORIGINAL)

16. The polypeptide of claim 15, wherein

(i) position 1 of each repeated triplet is deoxyadenosine or deoxyguanosine;

(ii) position 2 of each repeated triplet is deoxycytidine or deoxyguanosine; and

(iii) position 3 of each repeated triplet is deoxythymidine.

CLAIM 17 (ORIGINAL)

17. The polypeptide of any one of claims 3 or 11-16 in solution.

CLAIM 18 (ORIGINAL)

18. The polypeptide of any one of claims 3 or 11-16 adsorbed to, bound to, or integrated into, a carrier or delivery system.

CLAIM 19 (ORIGINAL)

19. The polypeptide of any one of claims 3 or 11-16, wherein said immune response is a protective anti-tumor immune response.

CLAIM 20 (ORIGINAL)

20. The polypeptide of any one of claims 3 or 11-16 that, upon administration to a mammalian host, including said subject, induces a polyclonal anti-idiotypic antibody response or a cell mediated immune response.

CLAIM 21 (ORIGINAL)

21. The polypeptide of claim 20 wherein the host is a human and said polyclonal anti-idiotypic responses are detected by testing serum or peripheral blood cells of the host.

CLAIM 22 (ORIGINAL)

22. The polypeptide of claim 20 wherein the antibody response is measured in an enzyme immunoassay or by flow cytometry.

CLAIM 23 (ORIGINAL)

23. The polypeptide of claim 20, wherein said administration comprises subcutaneous immunization with at least about 15 μg of said polypeptide antigen three times about two weeks apart.

CLAIM 24 (AMENDED)

24. An individual-specific immunogenic product comprising a polypeptide that binds specifically to an idiotope produced by a method comprising the steps of:

(a) joining a nucleic acid encoding the first domain of the polypeptide to a nucleic acid encoding a first part of a linker to produce a first nucleic acid construct;

(b) joining the nucleic acid encoding a second part of the linker to a nucleic acid encoding the second domain of the polypeptide to produce a second nucleic acid construct;

(c) incorporating said first and said second constructs into a transient plant expression vector in frame so that, when expressed, the polypeptide bears the first and second domain separated by the linker;

(d) transfecting a plant with the vector so that the plant transiently produces the polypeptide; and

(e) recovering the polypeptide as a soluble, correctly-folded protein.

CLAIM 25 (ORIGINAL)

25. The product of claim 24 that is a scFv polypeptide wherein the first domain is the Ig V_H domain and the second domain is Ig V_L domain, both of which domains create an idiotype of the immunoglobulin of the B cell lymphoma, and wherein said product induces an idiotype-specific antibody or cell-mediated immune response directed to said lymphoma upon administration to a subject.

CLAIM 26 (ORIGINAL)

26. The product of claim 25, wherein the plant is a plant cell.

CLAIM 27 (ORIGINAL)

27. The product of any one of claims 24-26 in aqueous solution.

CLAIM 28 (ORIGINAL)

28. The product of any one of claims 24-26 adsorbed to, bound to, or integrated into, a carrier or delivery system.

CLAIM 29 (ORIGINAL)

29. A vaccine composition useful for inducing a tumor-specific immune response , comprising

(a) the polypeptide of any one of claims 3 or 13-16; and

(b) a pharmaceutically acceptable carrier or excipient.

CLAIM 30 (AMENDED)

CLAIM 31 (AMENDED)

CLAIM 32 (ORIGINAL)

32. A vaccine composition that induces a polyclonal immune response to an idiotype in a mouse, comprising

(a) the polypeptide of claim 28; and

(b) a pharmaceutically acceptable carrier or excipient.

CLAIM 33 (ORIGINAL)

33. The vaccine composition of claim 30 wherein the polypeptide is a scFv that includes the V_H and the V_L domains.

CLAIM 34 (ORIGINAL)

34. The vaccine composition of any one of claims 30, which, when administered to the subject in which said tumor originated, elicits a protective anti-tumor immune response.

CLAIM 35 (ORIGINAL)

35. The vaccine composition of claim 34, wherein said protective anti-tumor immune response is a polyclonal anti-idiotypic antibody response.

CLAIM 36 (ORIGINAL)

36. The vaccine composition of claim 34, wherein said protective anti-tumor immune response is a T cell-mediated anti-idiotypic response.

CLAIM 37 (ORIGINAL)

37. The vaccine composition of claim 29, further comprising an adjuvant.

CLAIM 38 (ORIGINAL)

38. The vaccine composition of claim 29, further comprising an immunostimulatory cytokine or a chemokine.

CLAIM 39 (ORIGINAL)

39. The vaccine composition of claim 38 wherein said cytokine is selected form the group consisting of interleukin 1, interleukin 2, interleukin 12, interleukin 18 and interferon-γ.

CLAIM 40 (ORIGINAL)

40. The vaccine composition of claim 29 in unit dosage form wherein said excipient is sterile saline and wherein each unit includes between about 0.1 mg 10 mg of said polypeptide.

CLAIM 41 (ORIGINAL)

41. A method of inducing a tumor-specific immune antibody response in (i) a tumor-bearing subject or (ii) a subject who had a tumor and was treated so that no tumor is clinically or radiographically evident, comprising administering to said subject an effective amount of the vaccine composition of claims 29.

CLAIM 42 (ORIGINAL)

42. A method of inducing a tumor-specific immune antibody response in (i) a tumor-bearing subject or (ii) a subject who had a tumor and was treated so that no tumor is clinically or radiographically evident, comprising administering to said subject an effective amount of the vaccine composition of claims 33.

CLAIM 43 (ORIGINAL)

43. The method of claim 41 wherein the tumor Is B-cell lymphoma.

CLAIM 44 (ORIGINAL)

44. The method of claim 43, wherein the polypeptide is the scFv that includes at least part of the V_H and the V_L domains.

CLAIM 45 (ORIGINAL)

45. The method of claim 44, wherein the scFv polypeptide includes said V_H and the V_L domains.

CLAIM 46 (ORIGINAL)

46. The method of claim any one of claims 41-45, wherein said administering is by a parenteral route.

CLAIM 47 (ORIGINAL)

47. The method of claim 46, wherein said parenteral route is the subcutaneous, transdermal or intramuscular route.

CLAIM 48 (ORIGINAL)

48. A method of claim 41 wherein the polypeptide is in unit dosage form in aqueous solution at a concentration between about 0.1 and about 10 mg/ml.

CLAIM 49 (ORIGINAL)

49. The method of claim 41 wherein the subject is a human.

CLAIM 50 (ORIGINAL)

50. The method of claim 42 wherein the subject is a human.

CLAIM 51 (ORIGINAL)

51. A method of producing the polypeptide of any one of claims 13-16 comprising the steps of:

(a) joining a nucleic acid encoding the first domain of the polypeptide to a nucleic acid encoding a first part of a linker to produce a first nucleic acid construct;

(b) joining the nucleic acid encoding a second part of the linker to a nucleic acid encoding the second domain of the polypeptide to produce a second nucleic acid construct;

(c) incorporated said first and said second constructs into a transient plant expression vector in frame so that, when expressed, the polypeptide bears the first and second domain separated by the linker;

(d) transfecting a plant with the vector so that the plant transiently produces the polypeptide; and

(e) recovering the polypeptide as a soluble, correctly-folded protein.

CLAIM 52 (ORIGINAL)

52. The method of claim 51, wherein the polypeptide is a single chain wherein the first domain is the Ig V_H domain and the second domain is Ig V_L domain, both of which domains create an idiotype of a surface Ig of a B cell lymphoma, and wherein said product induces an idiotype-specific response directed to said lymphoma upon administration to a subject.

CLAIM 53 (ORIGINAL)

53. The method of claim 52 wherein the plant is a plant cell.

CLAIM 54 (new)

-- 54. The vaccine composition of claim 30 or 31 wherein said polypeptide is a single chain antibody.

CLAIM 55 (new)

55. The vaccine composition of claim 54 wherein the V_H and V_L domains of said single chain antibody are linked by an amino acid linker that

(a) has between about 1 and 50 residues;

(b) consists of between 1 and 12 different amino acids; and

(c) facilitates secretion and correct folding of said polypeptide to mimic the tumor epitope in its native form in or on said tumor cell.

CLAIM 56 (new)

56. The vaccine composition of claim 55 wherein said linker is a member of a randomized library of linkers that vary in size and sequence, and said library is encoded by nucleic acid sequences consisting of a repeated pattern of degenerate repeated triplet nucleotides having the following requirements:

(a) position 1 of each repeated triplet cannot be the same nucleotide as position 2 of the repeated triplet;

(b) position 2 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet; or

(c) position 1 of each repeated triplet cannot be the same nucleotide as position 3 of the repeated triplet.

CLAIM 57 (new)

57. The vaccine composition of claim 56 wherein the nucleotide in the first and second positions of each repeated triplet is selected from any two of deoxyadenosine, deoxyguanosine, deoxycytidine or deoxythymidine.

CLAIM 58 (new)

58. The vaccine composition of claim 57 wherein

(a) position one of each repeated triplet is deoxyadenosine or deoxyguanosine;

(b) position two of each repeated triplet is deoxycytidine or deoxyguanosine; and

(c) position three of each repeated triplet is deoxythymidine.--